A MECHANISTIC STUDY OF THE REACTIONS OF AZINES AND OTHER ANALOGOUS C=N SYSTEMS WITH SOME OXYGEN-TRANSFER AGENTS

By

RODRIGO PAREDES

A DISSERTATION PRESENTED TO THE GRADUATE SCHOOL OF THE UNIVERSITY OF FLORIDA IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA

1991

DEDICATED TO MY FOUR WOMEN,

Cielito, Jeanne, Ximena and Juliana,

and

TO THE MEMORY OF MY UNFORGETTABLE FRIEND,

Holger

ACKNOWLEDGEMENTS

It is with much gratitude that I acknowledge the guidance and advice of Professor William R. Dolbier, Jr. in my PhD endeavor. If it had not been for his encouragement and assistance, I would not have attained my PhD at such a late stage in my life. It was worth the effort and I enjoyed it very much.

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Abstract of Dissertation Presented to the Graduate School of the University of Florida in Partial Fulfillment of the Requirement for the Degree of Doctor of Philosophy

A MECHANISTIC STUDY OF THE REACTIONS OF AZINES AND OTHER ANALOGOUS C=N SYSTEMS WITH SOME OXYGEN-TRANSFER AGENTS

By

Rodrigo Paredes

December 1991

Chairman: William R. Dolbier, Jr.
Major Department: Chemistry

Treatment of imines with oxidizing agents leads to the formation of stable oxaziridines. Hydrazones, which can be viewed as imines with N bound to the C=N nitrogen, would be expected to form oxaziridines upon treatment with oxidizing agents. Our results indicate that the presence of N bound to the C=N nitrogen changes the course of the reaction and instead of an oxaziridine, a dipolar ion is formed as the first intermediate. Several products can derive from these dipolar ions depending on their nature and on reaction conditions. Azines, also imine analogs, should also form oxaziridines upon treatment with oxidizing agents. The evidence presented in this dissertation indicates that once again in this case, a dipolar ion is formed as the first intermediate instead of an oxaziridine. A common reaction of these dipolar ions is decomposition into carbonyl and diazo compounds. The latter can be further oxidized by excess oxidizing agent to a second carbonyl compound. In the presence of a

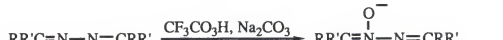
carboxylic acid, the diazo compound is trapped to generate the carboxylic acid ester. A synthetic application of this reaction is the selective reduction of one carbonyl group in open-chain dicarbonyl compounds. The strategy involves the initial conversion of the dicarbonyl compound into cyclic azine. The azine is then treated with an appropriate oxidizing agent in the presence of excess of a suitable carboxylic acid to give a ketoester as final reduced species. Phenyl-substituted azines treated with oxidizing agents form aromatic azine monoxides in competition with formation of the carbonyl compound. These monoxides can be derived either from the intermediate oxaziridine or by direct electrophilic attack of the oxidizing agent on the azine nitrogen. The evidence presented in this dissertation is consistent with the latter mechanism.

CHAPTER 1
OXIDATION OF AZINES TO AZINE MONOXIDES

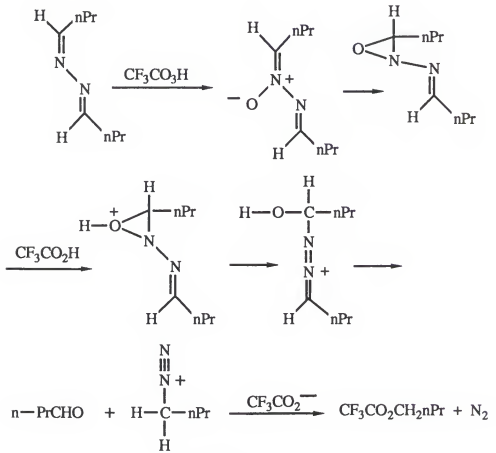
The peracid oxidation of azines to the various products observed has not been studied from a mechanistic point of view. Therefore, we thought it would be worth the attempt for this study. The aim of the work in this dissertation is to try to gain understanding of the chemistry involved in the oxidation of azines and other analogous C=N systems with various oxygen-transfer agents.

Our research group has been interested in the thermal reactivity and photochemistry of azine monoxides for a long time.[1,2] Thus, we have been interested in new, potentially useful oxygen-transfer reagents for the syntheses of azine monoxides from azines. In this regard, it was found that buffered trifluoroperacetic acid was useful in the preparation of a number of phenyl substituted azine monoxides, i.e. **2a** and **2b**, while for the alkyl-substituted analogues, only decomposition products were obtained (Scheme 1).[1] Although no intermediate azine monoxide was able to be detected in the latter case, it was considered reasonable that one might have been formed and then undergone acid catalyzed decomposition to the products observed (Scheme 2).

Phenyl-substituted azine monoxides would be expected to be more stable due to the resonance stabilization provided by the phenyl group (Figure 1).



Scheme 1



Scheme 2

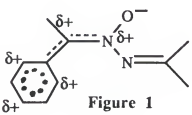
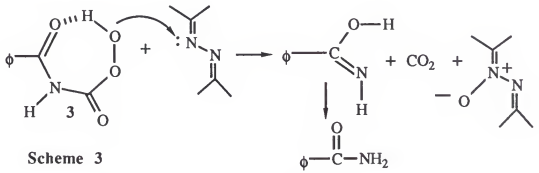


Figure 1

On the basis of our visualization of the reaction, we concluded that if the presence of acids could be avoided, the conversion of alkyl-substituted azine monoxides to undesirable products might well be prevented and thus these elusive azine monoxides could be prepared. Therefore, we became interested in searching for an effective oxidizing agent for acid-sensitive systems.

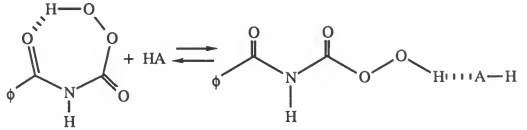
Oxidation of azines with N-benzoylperoxycarbamic acid. N-benzoylperoxycarbamic acid (BPC) was reported by Rebek and others to be an effective epoxidation agent with the advantage over typical peracids that it yields as co-products only neutral moieties.[3] This made it a potentially very useful reagent for dealing with possible acid-sensitive systems such as our alkyl-substituted azine monoxides. At that point we viewed the reaction of BPC with azines to produce azine monoxides as an electrophilic attack by the hydroxy oxygen of BPC **3** on a nitrogen lone pair of the azine (Scheme 3).



Scheme 3

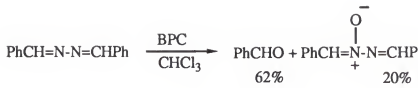
Like other hydroperoxy oxygen-transfer agents, BPC is very sensitive to the medium of reaction, being 200 times more reactive in aprotic solvents such as $CHCl_3$ than it is in hydrogen-bonding solvents such as THF or alcohols.[3] The higher reactivity in aprotic solvents can be attributed to a more ready oxygen-transfer action

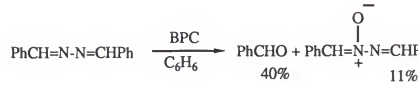
in the cyclic hydrogen bonded structure than in the open-chain structure (Scheme 4).[3,4,5]



Scheme 4

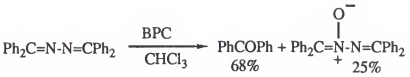
Therefore, most of our reactions were carried out in $CHCl_3$, generally reacting the azines with aliquots of crystalline BPC until reaction was complete (no further gas evolution). The results obtained are shown in Scheme 5. Contrary to what we expected, azine monoxide formation was not the prevalent pathway followed for any of the azines studied. Not even benzaldehyde and benzophenone azines which had given high yields of the respective azine monoxides when treated with CF_3CO_3H, provided good yields. In all reactions the azine precursor carbonyl compound(s) formed in varying amounts and in some cases unexpected "strange" products were also formed. This last fact seems to imply that the reactions proceed via a different, more complex mechanism than the one we had expected.

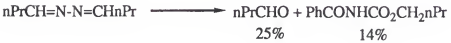

PhCH=N-N=CHPh
BPC
CHCl3
PhCHO + PhCH=N-N=CHPh
62%
20%


PhCH=N-N=CHPh
BPC
C6H6
PhCHO + PhCH=N-N=CHPh
40%
11%

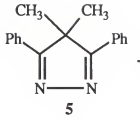

PhCH=N-N=CHPh
BPC
THF / reflux
PhCHO + PhCO-N=N-COPh + PhCO2CH2Ph
8%
4
50%
26%


Ph2C=N-N=CPh2
BPC, CHCl3
CF3CO2H
PhCOPh + Ph2C=N-N=CPh2 + Ph2CHOCOCF3
53%
9%
62%


Ph2C=N-N=CPh2
BPC
CHCl3
PhCOPh + Ph2C=N-N=CPh2
68%
25%


nPrCH=N-N=CHnPr
nPrCHO + PhCONHCO2CH2nPr
25%
14%

Scheme 5



5

$$\xrightarrow[CHCl_3]{BPC} PhCOC(CH_3)_2COPh\ (26\%) + PhCONH\text{-}N{=}CPh\text{-}C(CH_3){=}CH_2\ (21\%)\quad \mathbf{6}$$

$$Ph_2C{=}N\text{-}N{=}CMe_2 \xrightarrow[CHCl_3]{BPC} Ph_2CO + Me_2CO$$

$$Ph_2C{=}N\text{-}N{=}CMe_2 \xrightarrow[PhCO_2H]{BPC,CHCl_3} Me_2CO + PhCO_2CHPh_2\ (100\%)$$

$$Ph_2C{=}N\text{-}N{=}CHPh \xrightarrow[CHCl_3]{BPC} Ph_2C{=}\overset{O^-}{N^+}{-}N{=}CHPh\ (+\ 23\%) + Ph_2CO\ (76\%) + PhCHO\ (74\%)$$

$$Ph_2C{=}N\text{-}N{=}CHPh \xrightarrow[PhCO_2H]{BPC,CHCl_3} Ph_2C{=}\overset{O^-}{N^+}{-}N{=}CHPh\ (+\ 21\%) +$$

$$Ph_2CO\ (10\%) + PhCHO\ (70\%) + Ph_2CHO_2CPh\ (66\%) + PhCH_2O_2CPh\ (10\%)$$

Scheme 5--continued

CHAPTER 2
MECHANISTIC INTERPRETATIONS OF THE OXIDATIONS OF AZINES

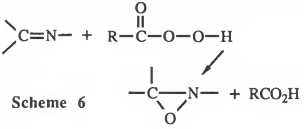
Azines and imines are structurally related compounds since both possess the C=N group. Therefore, it seemed reasonable that both would show similar mechanisms in their oxidation reactions. Since the oxidation by various peracids of imines has been studied,[4,6,7,8] it was considered important to understand the chemistry involved as some of the mechanistic aspects might be common to both oxidation reactions. Most imines are converted to oxaziridines when treated with peracids. Two mechanisms have been proposed for the formation of oxaziridines by the peracid oxidation of imines:

A. The one-step mechanism in which the π electrons of the C=N perform a nucleophilic attack on the hydroxylic oxygen of the peracid in a manner analogous to that suggested for the epoxidation of olefins (Scheme 6).[6,7]

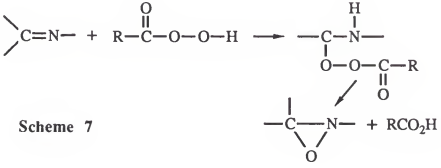
B. The two-step mechanism in which the hydroxylic oxygen of the peracid performs a nucleophilic attack on the imine carbon to form an adduct (Baeyer-Villiger type) which by an internal nucleophilic reaction affords the oxaziridine (Scheme 7).[4,8]

The oxidation reaction of imines to form oxaziridines is accelerated by protic solvents or by the presence of carboxylic acids. Madan and Clapp[7] explain this acceleration on

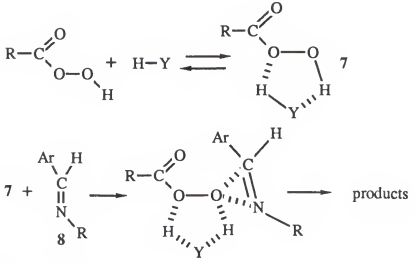
the basis of the initial formation of hydrogen-bonded complex **7** which then reacts with the imine **8** to yield the products (Scheme 8). Ogata and Sawaki[4] postulate that the acid catalysis is due to the hydrogen bonding at the imine nitrogen since acid-catalyzed addition of nucleophiles to C=N is well known (Scheme 9).[9,10]



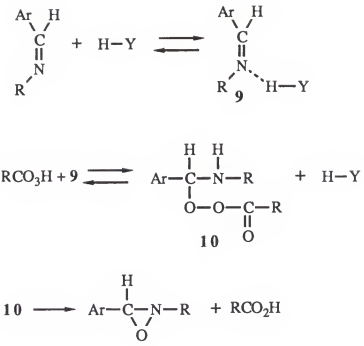
Scheme 6



Scheme 7

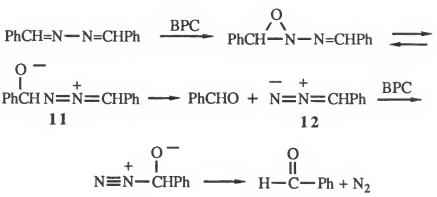


Scheme 8



Scheme 9

Oxidation of Azines with BPC. A likely pathway for the observed carbonyl formation in the reaction of azines with BPC involves initial formation of an oxaziridine,[11] in a manner analogous to the peracid reaction with imines. In the azine reaction, however, the oxaziridine proves to be unstable, decomposing via N-O cleavage to form a dipolar species such as **11** which can easily be converted to the carbonyl compound and a diazo species such as **12**. Indeed, there are no reports in the literature of stable oxaziridines which have donor electron pairs on the N atoms. The diazospecies **12** in the presence of excess BPC would not be expected to survive but would also be oxidized to carbonyl compound. The mechanism is depicted below for benzaldehyde azine (Scheme 10).

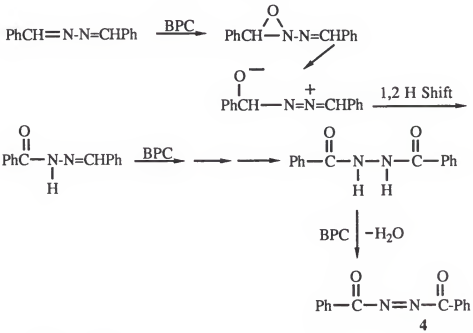


Scheme 10

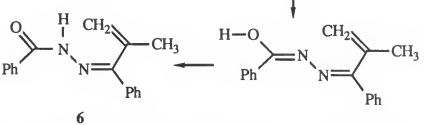
In an initial test of this mechanism, the oxidation reaction of an azine (benzophenone azine) was carried out in the presence of an excess carboxylic acid (trifluoroacetic acid) wherein benzhydryl trifluoroacetate was formed instead of a second molecule of the carbonyl compound (benzophenone). This result is explained in terms of the trapping of the intermediate diazo compound by the added carboxylic acid (Scheme 11). The formation of "strange" products such as benzoyldiimide **4** and hydrazide **6** in some of the azine oxidations, can also be explained on the basis of initially formed oxaziridines (Scheme 12). Our original idea that the oxaziridines might be derived from the azine monoxides and converted to products via acid catalyzed decomposition was not compatible with the results of this preliminary study in view of the stability of some azine monoxides to reaction conditions.[11] For example, when a THF solution of benzaldehyde azine monoxide and acetic acid was refluxed, it was observed that no reaction took place after six hours. Benzophenone azine oxide was relatively stable to acid and converted to benzophenone and

benzhydryl trifluoroacetate only slowly when treated with trifluoracetic acid/CH_2Cl_2 (34% conversion after 15 hours).

Scheme 11



Scheme 12



The azine oxide product, which is usually formed in competition with the carbonyl product, could derive from direct formation via reaction with the nitrogen

lone pair, or via competitive C-O bond cleavage of the intermediate oxaziridine. The results obtained in the oxidation of the mixed azine of benzophenone and acetone with BPC in the presence and in the absence of benzoic acid seemed to favor the latter explanation. The only products observed in the oxidation of the mixed azine with BPC were benzophenone and acetone with no formation at all of N-oxide (Figure 2) in spite of the presumption that it should be stable. The products formed in the oxidation of the mixed azine with BPC in the presence of benzoic acid were acetone and benzhydryl benzoate with no formation at all of benzophenone and isopropyl benzoate. This result clearly indicates specific oxidation at the azine side with the two methyl groups with the result that diphenyldiazomethane would be specifically formed and trapped by the benzoic acid to generate the ester. The lack of N-oxide product is consistent with all oxaziridine formation occurring specifically at the azine side with the two methyls followed by specific N-O cleavage of the resultant oxaziridine **13** to form the dipolar species **14** (Scheme 13) which is the precursor of the products. The specific decomposition of oxaziridine **13** can be explained on the basis of the decreased stability of potential azine oxide **15** (Scheme 14) due to the lack of phenyl substituents. Why did the attack take place specifically at the azine side with the two methyl groups? It is possible that the greater steric hindrance found on the side with the two phenyl groups drove the reaction to the other side. Also, the C=N π-bond is stabilized more by phenyl substituents than by methyl substituents and therefore the less-stabilized C=N π bond should be expected to be more reactive.

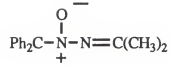
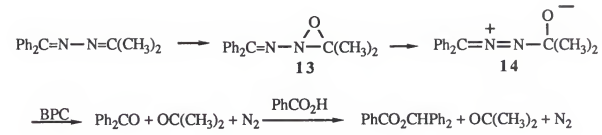
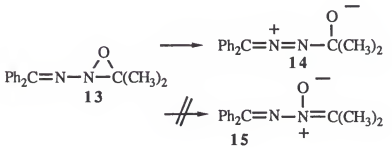


Figure 2



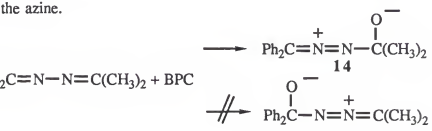
Scheme 13



Scheme 14

There is another plausible mechanistic explanation to the results observed in the oxidation of the mixed azine of benzophenone and acetone. One could hypothesize that specific attack at the azine side with the two methyl groups derives from direct formation of the dipolar ion **14** instead of the reaction proceeding via the oxaziridine. Resonance stabilization of the positive charge by the two phenyl groups could well give rise to the specific formation of dipolar ion **14** (Scheme 15). Analogous dipolar ions as **14** appear on previous schemes to explain the formation of the various products in the oxidation of azines. However, in these cases we had

viewed their formation as deriving from precursor oxaziridines. It may actually be that such azine-derived oxaziridines were not able to be detected simply because they did not form, and the reaction instead proceeded via direct formation of dipolar ions such as **14**. It should be clear that if the carbonyl compounds derive from azines by such a mechanism then azine monoxide products, when they are formed at all, must derive from direct competitive electrophilic attack by the peroxyacid on a nitrogen lone pair of the azine.



Scheme 15

In a more subtle test of the selectivity of azine oxidation, the mixed azine of benzophenone and benzaldehyde was treated with BPC. Again carbonyl production dominated but some azine oxide was formed (Figure 3). When the reaction was carried out in the presence of excess benzoic acid, the ratio of carbonyl products (benzaldehyde:benzophenone, 7:1) and ester products (benzhydryl benzoate:benzyl benzoate, 6.6:1) clearly indicated a preferential oxidation at the N=CHPh side of the azine. If the oxaziridine mechanism applies, by inference it would follow that oxaziridine **16** must have been formed preferentially over oxaziridine **17**. On the other hand, if the dipolar ion mechanism applies, dipolar ion **18** formed preferentially over dipolar ion **19** (Figure 4). Once again in this case, both mechanisms can explain the

results in a logical way. Oxaziridine **16** would form preferentially over **17** because of a greater reactivity of the N=CHPh π-bond. Dipolar ion **18** would form preferentially over **19** because of a greater resonance stabilization of the positive charge afforded by the two phenyls. We have designed two experiments in order to try to distinguish which of the two mechanisms actually applies to the oxidation reaction of azines with BPC. These two experiments and their results are described in chapters 4 and 5. However, before these experiments are discussed, it is relevant to study the reactions of two imines and two hydrazones with BPC in the next chapter.

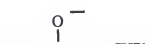


Figure 3

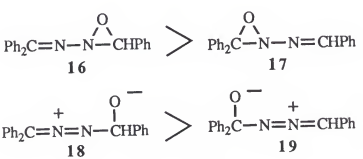
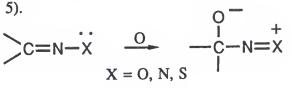


Figure 4

CHAPTER 3
OXIDATION OF 4-NITROBENZALDEHYDE-T-BUTYL IMINE,
4-METHOXYBENZALDEHYDE-T-BUTYL IMINE,
ACETONE METHYLPHENYLHYDRAZONE AND BENZALDEHYDE
METHYLPHENYLHYDRAZONE WITH N-BENZOYLPEROXYCARBAMIC ACID

Treatment of a wide variety of imines with peroxyacids generates stable oxaziridines in good yields.[6] However, there have been no reports of oxaziridines having been synthesized with electron-pair donor heteroatoms such as O, N or S bound to nitrogen. It seems plausible that in these cases no oxaziridines form and instead the first intermediates are dipolar ions similar to the ones proposed for azines (Scheme 16). If this hypothesis is valid, it would be expected that the BPC oxidation of imines **20** and **21** would generate oxaziridines while the BPC oxidation of hydrazones **22** and **23** would likely generate products derived from dipolar ion intermediates (Figure 5).



Scheme 16

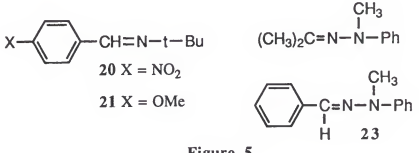
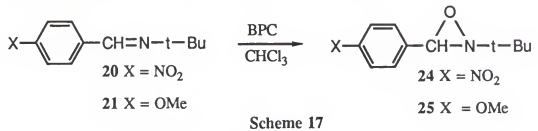


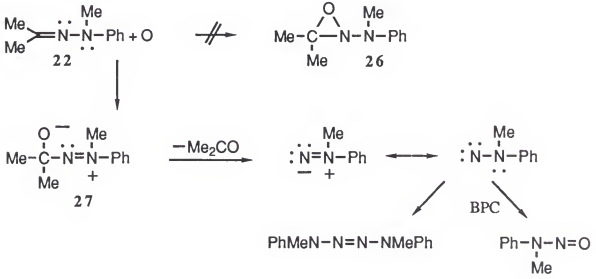
Figure 5

Treatment of imines **20** and **21** with BPC generated oxaziridines **24** and **25** as the only products (Scheme 17). It was found, using a 10-fold excess of each imine, that **21** reacted about two times faster than **20**. This result is consistent with the rate-determining step being an electrophilic attack on the imine.[11]



Scheme 17

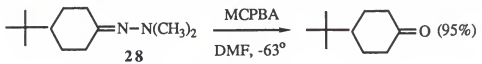
When hydrazone **22** was treated with BPC, no oxaziridine **26** could be detected and products appeared which might have been expected to have derived from dipolar ion **27** via a possible nitrene extrusion (Scheme 18).



Scheme 18

Duraisamy and Walborsky found that dimethyl hydrazones such as **28** are converted to their respective carbonyl species upon treatment with MCPBA[12] (Scheme

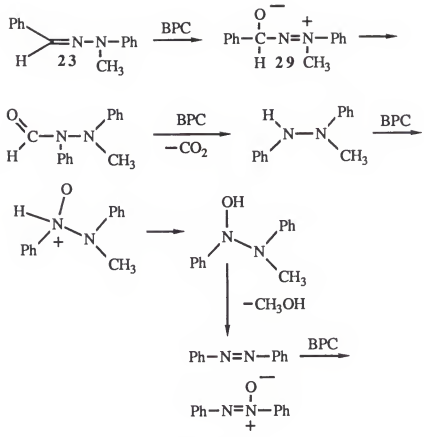
19). There are a number of other examples of peracid or hydrogen peroxide oxidations of hydrazone species which lead to carbonyl formation.[13-15] In all of these reactions, no oxaziridine intermediates could be detected. Presumably, the carbonyl compounds originate from dipolar ion intermediates analogous to **27**.



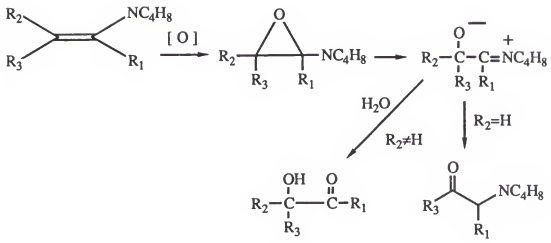
Scheme 19

Reaction of hydrazone **23** with an excess of BPC generated a compound which only showed ^{1}H NMR aromatic signals and no carbonyl absorption in the IR. This compound was identified as azoxybenzene (Figure 6) on the basis of its IR, ^{1}H NMR, ^{13}C NMR and mass spectra. Presumably, hydrazone **23** was converted into azoxibenzene via the corresponding dipolar ion **29** (Scheme 20). Vinylic compounds which are analogous to hydrazones such as **22** and **23**, are enamines in which the C=N group has been replaced by the C=C group. The oxidation of enamines to α-hidroxy ketones and α-amino ketones using N-sulfonyloxaziridines, has been explained by a mechanism involving the initial formation of an α-amino epoxide which rearranges to a dipolar ion, precursor of the products (Scheme 21).[16] However, attempts to detect the intermediate α-amino epoxides by NMR were unsuccessful[16] in spite of the fact that the synthesis of an α-amino epoxide has been reported.[17] This fact suggests that in the above reactions the dipolar ions were probably formed directly upon oxidation of the enamines.

Figure 6

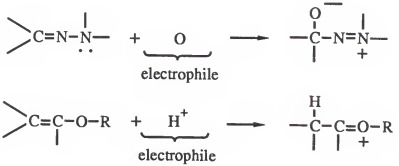


Scheme 20



Scheme 21

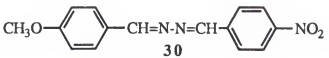
There is a close analogy between dipolar ion formation and the protonation of vinyl ethers (Scheme 22). In both cases the first intermediates formed are expected to be quite stable since all the atoms involved, except hydrogen, have their complete octets. The vinyl ether protonation reaction constitutes a valid precedent that makes the dipolar ion formation quite reasonable.



Scheme 22

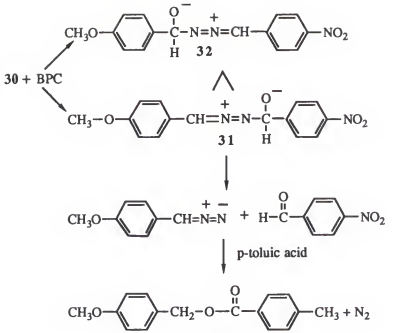
CHAPTER 4
OXIDATION OF N-4-NITROBENZYLIDEN-N'-4-METHOXYBENZYLIDENAZINE WITH N-BENZOYLPEROXYCARBAMIC ACID IN THE PRESENCE OF EXCESS p-TOLUIC ACID

It would seem reasonable that a study of the products formed in the BPC oxidation, in the presence of excess p-toluic acid, of a mixed azine with advantageous structural features such as **30**, might provide mechanistic insight into the nature of the reaction (Figure 7). In mixed azine **30**, the steric factor is quite similar on both sides of the molecule leaving the electronic factor to control the outcome of the reaction. If the reaction proceeds via dipolar ions, it would be expected that preferred formation of **31** over **32** would take place in view of the higher stability of the former dipolar ion. In this case, the main expected products would be p-nitrobenzaldehyde and p-methoxybenzyl p-toluate (Scheme 23). If, on the contrary, the reaction involves the initial formation of an oxaziridine, it would be expected that main products derived from **33** would be observed since oxaziridine formation is facilitated by electron release to the C=N group as observed in chapter 3 for the conversion of imines **20** and **21** into oxaziridines **24** and **25**. In this case, the main expected products would be p-methoxybenzaldehyde and p-nitrobenzyl p-toluate (Scheme 24).

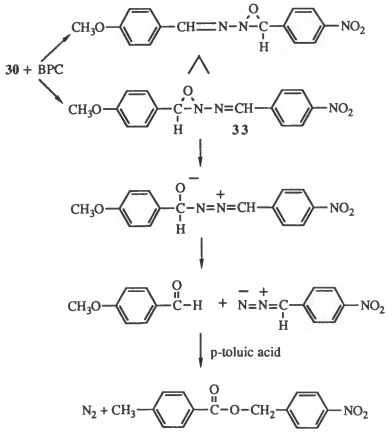


30

Figure 7



Scheme 23



Scheme 24

In the presence of excess toluic acid, 3.00 mmol mixed azine **30** was reacted at 40 °C with an excess of BPC in chloroform. After workup to remove unreacted toluic acid and benzamide, the solvent was taken off. The residue was then taken up in hexane filtering off an insoluble orange solid. Evaporation of the solvent left a residue which was dissolved in $CDCl_3$. Five main compounds appeared in this reaction mixture which were identified on the basis of the 300 MHz ^1H NMR spectrum. The yields of the compounds were determined using an internal standard as shown in Table 4-1. The results show that p-nitrobenzaldehyde and p-methoxybenzyl p-toluate form preferentially over p-methoxybenzaldehyde and p-nitrobenzyl p-toluate in about a 4:1 ratio as expected from the dipolar ion mechanism. The lower-than-expected p-nitrobenzaldehyde yield must be due to its facile oxidation to p-nitrobenzoic acid with the excess BPC.

The formation of p-methoxybenzyl p-nitrobenzoate as a minor product can be explained as deriving from diazo species and p-nitrobenzoic acid (Figure 8).

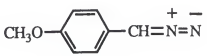
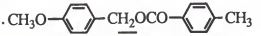
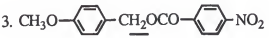
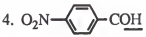
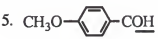
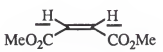


Figure 8

Table 4-1: Hexane Soluble Products in the Oxidation of N-4-Nitrobenzyliden-N'-4-methoxybenzylidenazine **30** with BPC in the Presence of Excess p-Toluic Acid

Compound	δ	Integral	% Yield
1. 	5.28	71.39	43.1
2. 	5.44	17.12	10.3
3. 	5.34	5.97	3.6
4. 	10.16	20.60	24.9
5. 	9.89	9.37	11.3
 internal standard (2,70 mmol)	6.26	148.99	

CHAPTER 5
OXIDATION OF N-CYCLOHEXYLIDEN-N'-4-NITROBENZYLIDENAZINE WITH N-BENZOYLPEROXYCARBAMIC ACID IN THE PRESENCE OF EXCESS p-TOLUIC ACID

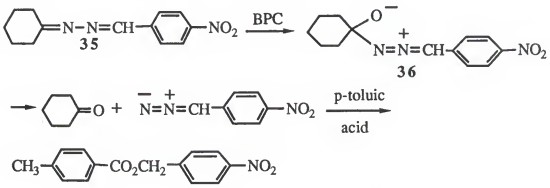
Most mixed azines are difficult to prepare in the pure form. One of the mixed azines we managed to prepare very pure was N-cyclohexyliden-N'-4-nitrobenzylidenazine **35**. It seemed reasonable that a study of the products formed in the BPC oxidation of **35**, in the presence of excess p-toluic acid, might provide further insight into the nature of the oxidation reaction of azines with peroxyacids.

In the presence of excess p-toluic acid, 0.408 mmol mixed azine **35** was reacted at room temperature in $CDCl_3$ with excess BPC. The insoluble solids were filtered off and 0.266 mmol 1,2-dibromoethane was added as an internal standard to the $CDCl_3$ solution. A 300 mHz ^1H NMR spectrum revealed that two main compounds had formed in the reaction: cyclohexanone and p-nitrobenzyl p-toluate. The respective yields were determined using the internal standard as shown in Table 5-1.

The results in Table 5-1 clearly indicate specific oxidation at the C=N carbon bearing the alkyl substituents (Scheme 25). This behavior is completely analogous to the BPC oxidation of the mixed azine of acetone and benzophenone in the presence of excess benzoic acid in which specific oxidation occurred at the carbon bearing the two

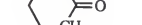
methyl groups. A reasonable explanation for the above result is that, of the two possible dipolar ions, **36** is much more stable than **37** due to the delocalization of the positive charge (Scheme 26).

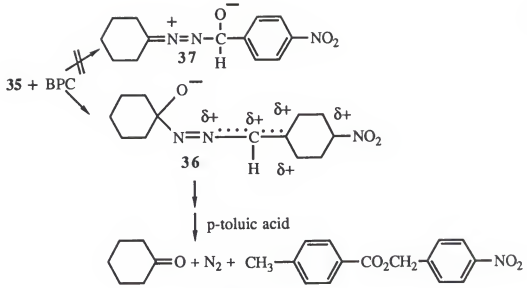
The BPC oxidation of the symmetrical azine of cyclohexanone in the presence of excess benzoic acid, leads to the clean formation of cyclohexanone and cyclohexyl benzoate as the only products. This result indicates that the analogous dipolar ion **37a**, precursor of the products, is a relatively stable intermediate not withstanding that the positive charge is not delocalized (Scheme 27).



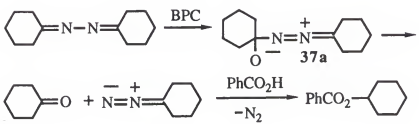
Scheme 25

Table 5-1: $CDCl_3$ Soluble Products in the Oxidation of N-Cyclohexyliden-N'-4-nitrobenzylidenazine **35** with BPC in the Presence of Excess p-Toluic Acid

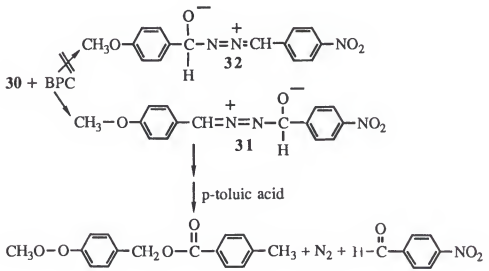
Compound	δ	Integral	% Yield
1. 	2.37	41.57	91.37
2. 	5.44	18.52	81.37
 (internal standard)	3.62	29.67	



Scheme 26



Scheme 27

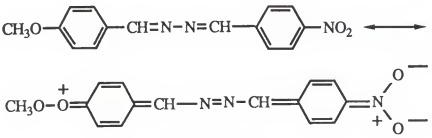


Scheme 28

It is interesting to observe that the destabilization due to the electron-withdrawal by the NO_2 group does not affect these reactions as much as might be expected. A large destabilization by the NO_2 group would have led to the specific formation of dipolar ion **31** in the BPC oxidation of mixed azine **30** (Scheme 28).

In the BPC oxidation of mixed azine **35**, a large destabilization by the NO_2 group would have led to products derived from both dipolar ions **36** and **37**.

An interesting observation was that mixed azine **35** reacted much faster than mixed azine **30** with BPC and p-toluic acid when both reactions were carried out at room temperature in $CHCl_3$. In the first case, gas evolution was brisk and the reaction was complete in less than 1 hour while in the second case, gas evolution was slow and the reaction was basically complete in 24 hours. If it is assumed that dipolar ion formation is the rate-determining step, the resonance stabilization of azine **30** would increase the stability of the reactant thereby diminishing its reactivity (Scheme 29).



Scheme 29

CHAPTER 6
OXIDATION OF SYMMETRICAL AZINES WITH N-BENZOYLPEROXYCARBAMIC ACID IN THE PRESENCE OF EXCESS OF A CARBOXYLIC ACID

A good number of symmetrical open-chain azines react with BPC in the presence of excess of a carboxylic acid to generate esters and carbonyl compounds in a clean reaction in which the yields of esters are generally high (Scheme 30).[18] The reaction seems to be general as shown in Table 6-1 (page 32). On the basis of our previous results, it seems that the reaction involves the formation of a dipolar ion followed by its decomposition to a carbonyl compound and a diazo compound which is trapped by the carboxylic acid to generate the ester.

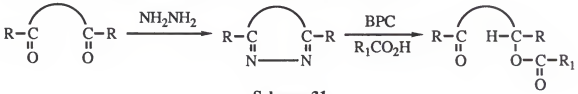
$$R_1R_2C{=}N{-}N{=}CR_1R_2 \;+\; PhCONHCO_3H \;+\; RCO_2H \longrightarrow$$

$$R_1R_2CHOCOR \;+\; N_2 \;+\; CO_2 \;+\; PhCONH_2 \;+\; R_1R_2CO$$

Scheme 30

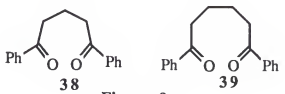
The selective reduction via cyclic azines of one carbonyl group in dicarbonyl compounds. The previous reaction, although clean and general, would not be an efficient synthetic method of esters $R_1R_2CHOCOR$ from carbonyl compounds R_1R_2CO via azines since for each mol of carbonyl compound, only half a mol of ester is produced. The situation is different for dicarbonyl compounds since in this case, both the carbonyl and the ester functional groups appear in the product. We

considered that in this case the reaction might be useful for the selective reduction of one carbonyl group in dicarbonyl compounds (Scheme 31). The classical method to perform this conversion involves the reduction of one carbonyl group to the alcohol followed by its esterification. However, in the first step, the stoichiometric control of the reducing agent, so as to reduce only one carbonyl, is an unreliable method.[19] Therefore, our proposed method might be more advantageous.



Scheme 31

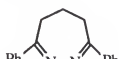
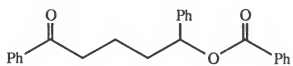
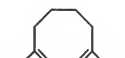
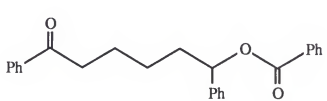
The method was tried employing dicarbonyl compounds **38** and **39** (Figure 9) with excellent results as shown in Table 6-2.



38 **39**

Figure 9

Table 6-2: Reactions of Symmetrical Cyclic Azines with BPC in the Presence of Excess Benzoic Acid

Azine	Esters Formed	% Yield
		82
		85

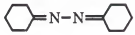
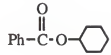
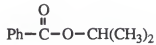
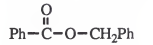
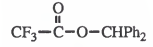
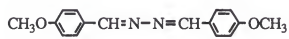
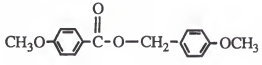
The proposed synthetic method has several advantages:

a. Cyclic azines form quite readily and in practically quantitative yields from dicarbonyl compounds and hydrazine.

b. The reaction of cyclic azines with excess BPC in $CHCl_3$ in the presence of excess carboxylic acid is quantitative.

c. The isolation of the ester product is quite simple since the unreacted BPC and carboxylic acid can be easily removed by filtration and by aqueous $NaHCO_3$ extraction. The side products are also easily removed: N_2 and CO_2 are gases and benzamide is removed by extracting the reaction mixture with hexane and filtering off the insoluble benzamide. Evaporation of the solvent leaves the desired ester quite pure.

Table 6-1: Reactions of Symmetrical Open-Chain Azines with BPC in the Presence of Excess Benzoic, Trifluoroacetic or p-Toluic Acids

Azine	Ester Formed	% Yield
		85
$(CH_3)_2C{=}N{-}N{=}C(CH_3)_2$		70
$PhC_2H_5C{=}N{-}N{=}CPhC_2H_5$		87
$PhHC{=}N{-}N{=}CHPh$		65
$Ph_2C{=}N{-}N{=}CPh2$		62
		61

CHAPTER 7
COMPARATIVE STUDY OF THE OXIDATION OF BENZALDAZINE WITH FIVE DIFFERENT OXYGEN-TRANSFER AGENTS

We have studied the chemical behavior of azines when treated with BPC. However, it was uncertain if this behavior remains the same when other oxygen-transfer agents are used. There are a wide variety of oxygen-transfer agents ranging from the more classical ones such as meta-chloroperbenzoic acid MCPBA, to the recently developed ones such as dimethyldioxirane **40**,[20-23] methyl(trifluoromethyl)-dioxirane **41**,[24] ortho-methoxybenzylazo-benzene-α-hydroperoxide **42**,[25,26] (±)-trans-2-phenylsulfonyl-3-phenyloxaziridine[27] **43** and 3-substituted 1,2-benzisothiazole 1,1 dioxide oxides[28] **44** (Figure 10).

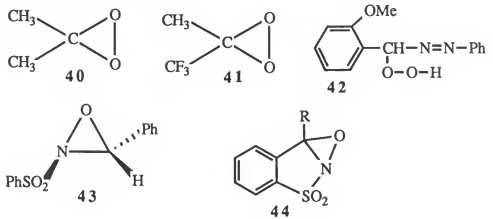


Figure 10

The natures of the various oxygen-transfer agents are different: MCPBA is a peroxycarboxylic acid, BPC is a peroxycarbamic acid, **40** and **41** are dioxirane species, **42** is an α-azohydroperoxide and **43** and **44** are sulfonyloxaziridines. However

different, all of the agents have in common the oxygen atom transfer capacity thereby acting as oxidants. All these agents are efficient epoxidizing agents of alkenes but display different reactivities. For example, the newly developed **41** is about 700 times more reactive than **40**.[22] More recently, Davis and coworkers found that 3-substituted 1,2-benzisothiazole 1,1-dioxide oxides 44 exhibit reduced reactivity and greater selectivity, compared to oxaziridines of type **43**, in their oxygen-transfer reactions (improved cis/trans selectivity for the epoxidation of (+)-limonene).[28]

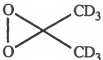
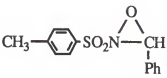
It was considered important to study the mechanistic behavior of azines upon oxidation with different oxygen-transfer agents; for example the possible relationship between reactivity and selectivity. One way to investigate this problem would be to react the same azine with different oxygen-transfer agents and to compare the nature and composition of the products formed. It is reasonable that if the same products are formed there is a strong indication that similar mechanistic pathways are being followed.

Table 7-1 shows the oxidation conditions employed for each of the five oxygen-transfer agents and the nature and composition of the products.

It is clear that in the reaction of benzaldazine with the five oxygen-transfer agents only two products derived from the azine were formed: benzaldehyde and benzaldazine monoxide. In the reactions carried out at room temperature, both products were formed with benzaldehyde predominating over benzaldazine monoxide in ratios that range between 3:1 to 2:1. In the reaction carried out at 50 °C, the only

product formed was benzaldehyde; while in the last reaction carried out at 0 °C, the major, if not exclusive, product was benzaldazine monoxide.[29]

Table 7-1: Products in the Oxidation of Benzaldazine with Five Oxygen-Transfer Agents

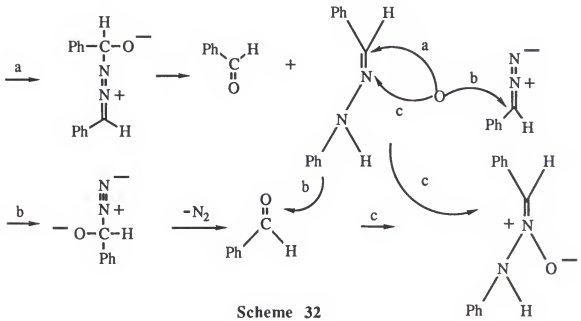
Oxidant	Conditions	Products	Composition
MCPBA	$CDCl_3$ (solvent) Room temp. H_2O,$NaHCO_3$	PhCHO O PhCH NNCHPh +	17% 9%
BPC	$CHCl_3$ (solvent) Room temp.	PhCHO O PhCH NNCHPh +	62% 20%
	$(CD_3)_2CO$ (solvent) Room temp.	PhCHO O PhCH NNCHPh +	33% 10%
	$CDCl_3$ (solvent) 50 °C	PhCHO O PhCH NNCHPh +	67% 0%
CF_3CO_3H	Et_2O (solvent) 0 °C H_2O,Na_2CO_3	PhCHO O PhCH NNCHPh +	--- 83%

On the basis of these results and of our previous mechanistic studies with BPC, it seems reasonable to conclude that the oxygen atoms liberated from the oxidants perform electrophilic attack on (Scheme 32):

a. one of the two C=N carbons of the azine to generate the dipolar ion intermediate.

b. the C=N carbon of the diazo compound, derived from the dipolar ion, to generate a second benzaldehyde molecule.

c. one of the two nitrogens of the azine to generate the azine oxide.



Scheme 32

CHAPTER 8
CONCLUSIONS

From a mechanistic point of view, azines behave differently than imines when treated with oxygen-transfer agents in spite of the fact that both possess the C=N group. New evidence presented by Davis and coworkers further support the two-step Bayer-Villiger type mechanism for the oxidation of imines to oxaziridines.[30] The evidence we have presented in this dissertation is consistent with the initial formation of dipolar ions in the oxidation if azines. Various types of products can result from these dipolar ions depending on their nature and on the reaction conditions. Their most common reaction is the decomposition into carbonyl and diazo compounds. The latter can in turn be oxidized by more oxygen-transfer agent to a second carbonyl compound molecule plus nitrogen. However, in the presence of a carboxylic acid, the diazo compound is preferentially trapped by the acid to generate an ester plus nitrogen. Another type of possible reaction carried out by the dipolar ions derived from aldehyde azines is hydride migration. The formation of benzoyldiimide upon BPC oxidation of benzaldazine involves hydride migrations on the initially formed dipolar ions.

Imines with donor heteroatoms such as N bound to the C=N nitrogen also behave mechanistically differently than common imines when treated with oxygen-transfer agents. The former behave similarly to azines undergoing electrophilic attack

by the liberated oxygen atoms to form dipolar ions as the first intermediates. Various types of products can also result from these dipolar ions. In the case of ketone hydrazones such as acetone methylphenylhydrazone, we found that the intermediate dipolar ions decompose to ketones and nitrenes which tend to couple to generate tetrazines. In the case of benzaldehyde methylphenylhydrazone **23**, the intermediate dipolar ion undergoes phenyl migration followed by decompositions and oxidations (excess BPC) to finally produce stable azoxybenzene.

The azine monoxides, which usually form in competition with the dipolar ions when phenyl-substituted azines are oxidized, result from direct electrophilic attack by the liberated oxygen atoms on the azines nitrogen lone pairs.

As a synthetic application of the oxidation of azines with oxygen-transfer agents, we found that in open chain dicarbonyl compounds the selective reduction of one carbonyl group can be achieved by conversion of the dicarbonyl compound to the cyclic azine followed by treatment with BPC in the presence of an excess of a carboxylic acid (Scheme 31).

A significant contribution of this work involves the new idea that treatment of doubly bonded compounds which have electron-pair donor heteroatoms such as O or N bound to one of the atoms of the double bond, with oxygen-transfer agents leads to the formation of dipolar ions as the first intermediates of the reaction. The compounds mentioned in this dissertation which seemed to display this behavior were azines, hydrazones and enamines. However, it is possible that other analogous compounds

such as vinyl ethers, might also show the same reaction pattern. This is an area worthy of further investigation, mainly from a mechanistic point of view.

Another contribution of our work is the proposed synthetic method for the selective reduction of one carbonyl group in open-chain dicarbonyl compounds. Further work in this area is also required in order to broaden the scope of the reaction. For example, in the case of unsymmetrical dicarbonyl compounds such as $RCO(CH_2)_nCOA$ or $HCO(CH_2)_nCOR$, it would be necessary to investigate which side of the molecule is preferentially reduced.

CHAPTER 9
EXPERIMENTAL SECTION

General Methods

Infrared (IR) spectra were taken as films between KBr plates or as CCl_4 solutions in 0.10 mm matched liquid cells. The IR spectra were taken on Perkin-Elmer 283B or 599B spectrophotometers and are reported in cm^{-1}.

Nuclear magnetic resonance (NMR) chemical shifts for ^{1}H and ^{13}C spectra are reported in parts-per-million downfield (δ) from internal TMS. Spectra were mostly taken in $CDCl_3$ or CCl_4. All NMR spectra were taken on a Varian T-60, Jeol FX-100, Jeol FX-90Q or a Nicolet NT-300 spectrometer.

Mass spectra and exact masses were determined on an AEI-MS 30 spectrometer at 70 eV. Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are uncorrected.

Experimental Procedures

Benzophenone azine (**1a**) reaction with BPC. Into a 25 mL, round-bottom flask equipped with magnetic stirrer and glass stopper were added 744 mg (2.06 mmol) 1a,[31] 10 mL $CHCl_3$, and 2.298 g (12.7 mmol) BPC. The yellow mixture was allowed to stir at ambient temperature for 19 hours. The reaction mixture was filtered to give a white solid and a yellow filtrate. The solid was washed with two 2-mL portions of $CHCl_3$. The combined filtrates were concentrated to give a yellow solid

which was then subjected to flash chromatography on silica gel, eluting with 20% ethyl acetate/80% hexane.

The first eluted compound was benzophenone. The yield was 509 mg (68%). The second eluted compound, amber solid, was identified as benzophenone azine monoxide. The yield was 195 mg (25%). Recrystallization from chloroform/hexane gave mp 148-151° (lit.[27] mp 157°): IR (KBr) 3060w, 3030w, 2480w, 1590w, 1565m, 1525m, 1490m, 1440m, 1315m, 1295w, 1240s, 1130m, 1075m, 970m, 760s, 690vs cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.56 (m, 2H), 7.47 - 7.36 (m, 6H), 7.33 - 7.24 (m, 10H), 7.08 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0 (C=N), 135.8 (quat), 134.3 (quat), 133.6 (quat), 133.1 (quat), 131.8 (CH), 130.8 (CH), 130.5 (CH), 129.9 (CH), 129.7 (CH), 129.1 (CH), 128.7 (CH), 128.2 (CH), 127.8 (CH), 127.7 (CH); MS (m/e) 376 (M^+, 5), 360 (13), 283(28), 196(11), 180(50), 165(100), 105(34), 77(69), 51(19).

Benzaldehyde azine (**1b**) reaction with BPC, NMR yield. Into a 10-mL beaker were added 55 mg (0.264 mmol) **1b**[32] and 2 mL $CDCl_3$. To the pale yellow solution were carefully added 259 mg (1.43 mmol) BPC a little bit at a time. The exothermic reaction liberates CO_2. The reaction had a short induction period. After addition was completed, 27.5 mg (0.376 mmol) DMF were added as an internal standard. Integration of the 60 MHz NMR spectrum gave 5.12 for the benzaldehyde proton and 35.4 for the DMF methyls. This translates to an NMR yield of 62% for the benzaldehyde.

Benzaldehyde azine reaction with BPC. Into a 25-mL round-bottom flask equipped with magnetic stirrer were added 800 mg (3.84 mmol) **1b** and 10 mL

$CHCl_3$. To the stirred solution were carefully added 2.50 g (13.8 mmol) BPC a little at a time. Gas was evolved and the flask became warm. After completion of addition, the solution was allowed to cool to ambient temperature and benzamide precipitated. The mixture was filtered and the solid washed with 2 mL chloroform. The combined filtrates were subjected to flash column chromatography using silica gel and eluting with 20% $CHCl_3$/50% hexane, and finally pure $CHCl_3$. The first compound to elute was an amber semi-solid (R_f=0.32). The second compound to elute was an amber semi-solid (R_f=0.12). A total of 175 mg (20%) of this compound was obtained. It was identified as benzaldehyde azine monoxide by comparison with a authentic sample. A second flash chromatography using $CHCl_3$, followed by recrystallization from hexane gave colorless needles mp 127-128° (lit.[27] mp 130-131°): IR (KBr) 1660, 1610, 1580, 1555, 1450, 1210, 1095, 1070, 820, 755, 690s cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.40 (1 H, s), 8.28 (2H, dd, J=2.1 and 7.3 Hz), 7.86 (3H, m), 7.44 (6H, m); MS (e/m) 224 (M^+, 1), 207(3) 131 (6), 103 (100), 90 (3), 76 (43), 51 (20); mean of eight scans is 224.0977 ± 0.00235 (± 10.5 ppm); Calc. mass for $C_{14}H_{12}N_2O$ is 224.09496 dev + 0.002824 (+ 12.6 ppm).

Butanal azine (1c) reaction with BPC. Into a 100-mL round-bottom three-necked flask equipped with magnetic stirrer, thermometer, nitrogen inlet and nitrogen outlet were added 800 mg (5.70 mmol) butanal azine[33] and 10 mL $CHCl_3$. The flask was cooled in an ice bath to 10°. To the flask were carefully added 1.138 g (6.28 mmol) BPC over a period of 10 minutes. The temperature remained below 15°. A gas was evolved. After addition was completed the mixture was allowed to warm to

room temperature and the solvent was removed by rotary evaporation at reduced pressure. The reaction mixture was subjected to flash chromatography using silica gel and eluting with 30% ethyl acetate/70% hexanes. A total of 76.6 mg (7.5%) clear, colorless liquid, which was butyl benzoate, were obtained (R_f=0.45): IR 3310w, 2955s, 2870m, 1630s, 1555m, 1445m, 1395m, 1325s, 1160m, 1070s, 780m, 690m cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.75 (2H, dd, J=1.7 and 8.0 Hz), 7.42 (3H, m) 4.26 (2H, t, J=6.6 Hz), 1.80 (2H, m), 1.51 (2H, m), 0.99 (3H, t, J=7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6 (C=0), 133.0 (quat), 130.8 (CH), 128.4 (CH), 126.7 (CH), 65.9 (CH_2O), 30.8 (CH_2), 19.4 (CH_2), 13.9 (CH_3); MS e/m 178 (M^+, 5), 122(88) 105 (100), 77 (48), 51 (23). In addition, 175 mg (14%) N-benzoylcarbamic acid butyl ester were obtained as a colorless solid which was recrystallized from hexane/$CHCl_3$ to give a colorless solid mp 55-59° (R_f=0.25): IR (KBr) 3250s(br), 2970m, 2880w, 2410w, 1755s, 1685m, 1520s, 1200s, 1155w, 1055m, 1020m, 955m, 777m, 705 m cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.86 (1H, s), 7.90 (2H, d, J=7.0 Hz), 7.55 (1H, t, J=7.5 Hz), 7.44 (2H, t, J=7.4 Hz), 4.18 (2H, t, J=6.7 Hz), 1.62 (2H, m), 1.37 (2H, m), 0.90 (3H, t, J-7.4 Hz), ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4 (C=0), 151.6 (C=0), 133.1 (quat), 132.9(CH), 128.7 (CH), 127.9 (CH), 66.0 (CH_20), 30.6 (CH_2), 18.9 (CH_2), 13.6 (CH_3) MS e/m 221 (M^+, 5), 193(2), 166 (52), 149 (3), 121(4), 105 (100), 77(54), 56 (14), 51 (19).

Butanal azine reaction with BPC, NMR yield. Into a 10-mL beaker were added 100 mg (0.713 mmol) butanal azine and 1.0 mL $CDCl_3$. To the solution were carefully added 194 mg (1.07 mmol) BPC. The reaction was exothermic and gas was

envolved. After cooling to ambient temperature, 50 mg (0.331 mmol) p-nitrobenzaldehyde were added as internal standard. The solution was drawn up in a syringe and separated from solid benzamide. The 300 MHz ^1H NMR was taken and the resonances of the aldehyde protons were integrated to determine the yield. Integrations of 1.4280 for p-nitrobenzaldehyde and 1.5683 for butanal were obtained, indicating a yield of 0.363 mmol butanal (25%).

4,4-Dimethyl-3,5-diphenyl-4(H)-pyrazole reaction with BPC in chloroform. Into a 100-mL round-bottom flask equipped with magnetic stirrer were added 800 mg (3.22 mmol) of the cyclic azine[1] and 10.0 mL $CHCL_3$. To the stirred solution were carefully added 1.751 g (9.67 mmol) BPC a little bit at a time. There was a slight induction period before reaction occurred. A red-brown color appeared which faded at the end of addition. A gas was evolved and the flask became warm. After 30 minutes at ambient temperature, the excess BPC and benzamide were removed by suction filtration. The pale yellow filterate was concentrated by rotary evaporation at reduced pressure to give a mixture of yellowish solid and oil. Purification by flash chromatography gave 215 mg (25%) 2,2-dimethyl-1,3-diphenylpropane-1,3-dione (R_f=0.59) as a white solid mp 75-92°. Recrystallization from hexane gave colorless crystals mp 96.0-97.8° (lit[34] mp 99°): IR (CCl_4) 3060w, 2980w, 2920w, 1660s, 1590m, 1580m, 1250m, 940m cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.84 (4H, d, J=7.3 Hz), 7.38 (2H, t, J=7.3 Hz), 7.28 (4H, t, J=7.5 Hz) 1.66 (6H, s). There were also obtained 183 mg (21%) 1-(2-methyl-1-phenyl)propenylidene-benzoic acid hydrazide **6** (R_f=0.21) as a white solid mp 116.5 - 117.7°. Recrystallization from

hexane/$CHCl_3$ gave fine white needles mp 110.0-111.0° IR (CCl_4) 3350w, 3310w, 3070w, 3030w, 2930w, 1695s, 1665s, 1475s, 1450m, 1320s, 1250m, 1140m, 900m, 700s cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.56 (1H, s) 7.82, (4H, m), 7.47 (3H, m), 7.37 (3H, m), 5.72 (1H, s), 5.23 (1H, s), 1.96 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.3 (C=O), 156.45 (C=O), 137.8 (quat), 134.5 (quat), 133.5 (quat), 132.0 (CH) 130.0 (CH), 128.9 (CH), 128.5 (CH), 127.3 (CH), 127.1 (CH), 119.7 (=CH_2), 21.2 (CH_3); MS e/m 264 (M^+, 5) 223 (4), 159 (42), 105 (100), 77 (50), 51 (11). There were also obtained 44 mg white solid (R_f=0.28) mp 91-100°. Analysis by ^1H NMR indicated this to be a mixture of compounds even though it gave only one TLC spot. Recrystallization from hexane gave white solid mp 100-105.3°; however, no improvement in the purity was observed by ^1H NMR.

Benzaldehyde azine reaction with BPC in THF. Into a 100-mL, round-bottom flask equipped with magnetic stirrer were added 0.500 g (0.0024 mol) benzaldehyde azine and 5 mL dry THF. To the stirred solution were slowly added a mixture of 0.500 g BPC of 95% purity (0.0026 mol) and 5 mL dry THF. The mixture was stirred for two hours. TLC analysis showed the appearance of products and unreacted azine. After 16 hours of stirring at room temperature, the mixture had not changed much. The flask was equipped with a reflux condenser and the mixture was refluxed gently for one hour. The solvent was taken off in vacuo, the residue was taken up in hexane and the benzamide was removed by filtration. The hexane was taken off in vacuo and the mixture was separated by column chromatography on silica gel eluting with pentane-ether (8:1). The separation afforded 0.040 g benzaldehyde (8%), 0.300 g

benzoyldiimide (50%), 0.130 g benzyl benzoate (26%) and unreacted azine. Benzoyldiimide was identified on the basis of its ^{1}H NMR ($CDCl_3$) δ 7.5 (6H, m), 8.1 (4H, m); MS main fragments; m/e 28, 77, 105, 161, (M^+ does not appear) and mp 119-121° (lit[35] 119.5-121.5°). Benzyl benzoate was identified by comparison (IR and ^{1}H NMR) with an authentic sample.

Benzophenone azine (1a) reaction with BPC in the presence of trifluoroacetic acid. Into a 25-mL, round-bottom flask equipped with magnetic stirrer and nitrogen inlet stopcock, were added 800 mg (2.22 mmol) **1a**, 10 mL $CHCl_3$, 506 mg (4.44 mmol) trifluoroacetic acid, and 1.206 g (6.66 mmol) BPC. The yellow mixture was allowed to stir at ambient temperature for 17 hours. The insoluble white solid was removed by suction filtration and washed with 1 mL $CHCl_3$. The $CHCl_3$ solution was concentrated by rotary evaporation at reduced pressure to give a mixture of liquid containing a pale yellow solid. The mixture was purified by flash chromatography using silica gel and eluting with 20% ethyl acetate/80% hexane. A total of 74.2 mg (9%) pale yellow solid benzophenone azine oxide (R_f=0.46) were obtained. There were also obtained 810 mg pale yellow liquid (R_f=0.73) which was a mixture of benzophenone and benzhydryl trifluoroacetate, which could not be further separated by chromatography. Analysis by ^{1}H NMR (300 MHz, $CDCl_3$) was performed. The amount of benzophenone was determined by integration of the aromatic resonance at 7.76 ppm, while the benzhydryl trifluoroacetate was determined by integration of the benzhydryl methine resonance at 6.96 ppm. In the mixture, there were 426 mg (53%) benzophenone and 384 mg (62%) benzhydryl trifluoroacetate.

N-Isopropylidene-N'-diphenylmethyleneazine reaction with BPC. The mixed azine[36] was dissolved in $CDCl_3$ in an NMR tube and BPC was added in small portions to the solution. Reaction was immediate with the liberation of gases. The reaction was monitored by ^1H NMR with the result that as the methyl hydrogen signal of the azine disappeared, the methyl hydrogen signal of acetone appeared. Sufficient BPC was added to consume all the azine and then the $CDCl_3$ and the acetone were taken off in vacuo. The residue was taken up in CCl_4 and the benzamide was removed by centrifugation. ^1H NMR analysis of the CCl_4 solution showed that benzophenone was the only solute present.

N-Isopropylidene-N'-diphenylmethylenazine reaction with BPC in the presence of benzoic acid. The mixed azine and benzoic acid were dissolved in $CHCl_3$ in 1:2 molar ratio. Solid BPC was added in portions to the solution until all the azine was consumed. During the reaction, the solution turned red and gases were given off. The solution was extracted with aqueous $NaHCO_3$ until all benzoic acid was removed and then it was dried with Na_2SO_4. The solvent was taken off in vacuo, the residue was taken up in CCl_4, and the benzamide was separated by filtration. Then the CCl_4 was taken off in vacuo and the residue was recrystallized from ethanol to yield white needles with a sharp melting point of 88°. This compound was identified as diphenylmethyl benzoate (lit.[37] mp 88-89°): ^1H NMR (60 MHz) δ 8.2 (2H, m), 7.4 (14H, m).

N-Benzylidene-N'-diphenylmethyleneazine reaction with BPC. The mixed azine[38] was dissolved in $CHCl_3$ and BPC was added in small portions to the solution.

Reaction was immediate with the liberation of gases. Sufficient BPC was added to consume all of the azine and then the solvent was taken off in vacuo. The residue was taken up in CCl_4 and the benzamide was removed by filtration. Analysis of the filtrate by TLC and ^1H NMR showed that it was made up of benzophenone, benzaldehyde and azine monoxide as solutes. The yields were 76% for benzophenone, 74% for benzaldehyde and 23% for the azine monoxide. For the azine monoxide: ^1H NMR (60 MHz, CH_2Cl_2) δ 9.4 (1H, s), 8.0 (2H, m), 7.4 (13H, m). The structure of this azine monoxide had been unambiguously established.[29]

N-Benzylidene-N'-diphenylmethyleneazine reaction with BPC in the presence of benzoic acid. The mixed azine and benzoic acid were dissolved in $CHCl_3$ in a 1:2 molar ratio. Solid BPC was added to the solution in portions until all the azine was consumed. During the reaction the solution turned reddish and gases were given off. The solution was extracted with aqueous $NaHCO_3$ until all the benzoic acid was removed and then it was dried with anhydrous Na_2SO_4. The solvent was taken off in vacuo, the residue was taken up in CCl_4 and the benzamide was separated by filtration. Analysis of the filtrate by TLC and ^1H NMR showed that the solutes present were azine monoxide (Figure 19), benzophenone, benzaldehyde, diphenylmethyl benzoate and benzyl benzoate. The yields were 21% for the azine monoxide, 10% for benzophenone, 70% for benzaldehyde, 66% for diphenylmethyl benzoate and 10% for benzyl benzoate.

Benzophenone azine oxide (2a) reaction with trifluoroacetic acid. Into a 10-mL, screw-cap vial were added 68.4 mg (0.600 mmol) trifluoroacetic acid, 1.0 mL

CH_2Cl_2, and 112.9 mg (0.300 mmol) **2a**. After 15 hours at ambient temperature, the solvent was removed by rotary evaporation at reduced pressure to give 159.2 mg pale yellow oil which was redissolved in 10.0 mL $CHCl_3$, washed three times with 5.0 mL portions 15% aq. sodium carbonate, dried over anhyd. sodium sulfate and concentrated by rotary evaporation at reduced pressure to give 110.0 mg pale yellow oil containing some solid. The ^1H NMR (300 MHz) was taken. Integration of the benzophenone aromatic resonance at 7.80 ppm, the benzophenone azine oxide aromatic resonance at 7.07 ppm, and the benzhydryl trifluoroacetate benzhydryl resonance at 6.98 ppm gave the relative amounts of each compound. There were obtained 23% benzophenone, 11% benzhydryl trifluoroacetate, and there remained 66% benzophenone azine oxide.

Benzaldehyde azine (**1b**) reaction with BPC in Benzene, NMR yield. Into a 5-mL, round-bottom flask equipped with magnetic stirrer and glass stopper were added 100 mg (0.480 mmol) **1b**, 2 mL benzene-d_6, and 261 mg (1.44 mmol) BPC. The yellow mixture was allowed to stir for 46 hours at ambient temperature. To the mixture were added 57 mg (0.780 mmol) DMF. The mixture was filtered and the 60 MHz ^1H NMR of the filtrate was taken. The integration for the benzaldehyde proton was 5.8 and the DMF methyl groups were 70.0. This works out to an NMR yield of 40% for benzaldehyde.

Benzaldehyde azine reaction with BPC in benzene. Into a 100-mL, round-bottom flask equipped with magnetic stirrer and glass stopper were added 800 mg (3.84 mmol) **1b** and 10 mL benzene. To the clear, yellow solution were carefully added 2.50 g (13.8 mmol) BPC. Only a little BPC was added at first and since no

reaction occurred over a 20-minute period, the flask was heated gently with a hot air gun. Gas was evolved as the reaction proceeded. Heating was discontinued and addition of BPC was maintained to keep the reaction going. The reaction was strongly exothermic. After addition was completed, the reaction mixture was allowed to stir at ambient temperature for 46 hours. The mixture was filtered and the white solid washed with 2 mL benzene.

The combined filtrates were subjected to flash column chromatography on silica gel eluting with 50% $CHCl_3$/50% hexane. The product was eluted when the solvent was switched to pure $CHCl_3$. A total of 97.7 mg (11%) yellow solid was obtained. The yellow solid was determined to be benzaldehyde azine monoxide (**2b**) by comparison with an authentic sample.[29]

4-Methoxybenzaldehyde-t-butyl imine syntheses. Into a 100-mL flask were added 30 mL t-butylamine (0.286 mol) and 1.36 g (0.0100 mol) 4-methoxybenzaldehyde. The mixture was refluxed for 10 hours and then the unreacted t-butylamine was taken off in vacuo. The residue was dissolved in 10 mL chloroform and dried with anhydrous Na_2SO_4. Then the solvent was removed by rotary evaporation. 1.80 g of 4-methoxybenzaldehyde-t-butyl imine were formed (94% yield): ^{1}H NMR (60 MHz, CCl_4) δ 8.1 (1H, s), 7.6 (2H, m), 6.8 (2H, m), 3.6 (3H, s), 1.2 (9H, s).

4-Nitrobenzaldehyde-t-butyl imine syntheses. Into a 100-mL flask were added 30 mL t-butylamine (0.286 mol) and 1.51 g (0.0100 mol) 4-nitrobenzaldehyde. The mixture was refluxed for five hours and then the unreacted t-butylamine was taken off

in vacuo. The residue was dissolved in 10 mL chloroform and dried with anhydrous Na_2SO_4. Then the solvent was removed by rotary evaporation. 2.01 g of 4-nitrobenzaldehyde-t-butyl imine (98% yield) were formed: ^1H NMR (60 MHz, CCl_4) δ 8.3 (3H, m), 7.9 (2H, m), 1.35 (9H, s).

Benzaldehyde methylphenylhydrazone syntheses. Into a three-necked, 1-L flask equipped with a mechanical stirrer, reflux condenser and stopper, were added 500 mL 95% ethanol, 25.0 g (0.205 mol) methylphenylhydrazine[39] and 25.0 g (0.236 mol) benzaldehyde. The mixture was refluxed for two hours and then allowed to stand overnight in the refrigerator. The hydrazone was separated as a pale yellow solid by filtration and then allowed to dry. The yield was 31.5 g (73.2%) of the hydrazone with m.p. 104 °C. The ^1H NMR spectrum was: (300 MHz, $CDCl_3$) δ 7.66 (2H, m), 7.31 (8H, m), 6.85 (1H, m), 3.28 (3H, s).

N-4-Nitrobenzylidene-N'-cyclohexylidenazine syntheses. Into a 50-mL, round-bottom flask equipped with magnetic stirrer was added a solution of 2.94 g (0.0300 mol) cyclohexanone dissolved in 10 mL isopropyl alcohol. While stirring at room temperature were added in portions 1.65 g (0.0100 mol) p-nitrobenzaldehyde hydrazone. The mixture was stirred at room temperature for four hours. The mixture was then cooled in an ice bath and the yellow solid was filtered. The crystals were washed with cold ethanol and dried in the air. Yield 1.76 g (72%) m.p. 93°: ^1H NMR (300 MHz, $CDCl_3$) δ 8.37 (1H, s), 8.27 (2H, m), 7.94 (2H, m), 2.72 (2H, m), 2.44 (2H, m), 1.77 (6H, m). IR (Nujol mull) 1660 m, 1540 s, 1480 s, 1370 s, 1140 m, 880 m cm^{-1}.

N-4-Methoxybenzylidene-N'-4-nitrobenzylidenazine syntheses. Into a 100-mL, three-necked flask equipped with magnetic stirrer, condenser and dropping funnel were added 0.100 g (6.1×10^{-4} mol) p-nitrobenzaldehyde hydrazone and 10 mL ethanol. While stirring at room temperature were added dropwise 0.74 mL (6.0×10^{-3} mol) anisaldehyde dissolved in 5 mL ethanol. Reaction was immediate with the formation of a yellow solid. The mixture was refluxed for two hours and then it was left standing at room temperature overnight. Some of the ethanol was taken off in vacuo and then the yellow crystals were separated by filtration. The crystals were washed three times with cold ethanol and dried. Yield 0.17 g (100%) mp 202°: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.72 (1H, s), 8.67 (1H, s), 8.3 (2H, d), 8.0 (2H, d), 7.85 (2H, d), 7.0 (2H, d), 3.9 (3H, s); MS e/m 283 (M+, 90), 256 (40), 176 (52), 161 (80), 134 (45), 92 (55), 77 (100), 64 (31), 51 (38).

Nitrobenzaldehyde-t-butyl imine (**20**) reaction with BPC. Into a 25-mL, round-bottom flask equipped with magnetic stirrer were added 812 mg (3.94 mmol) **20** and 10 mL $CHCl_3$. To the solution were carefully added 876 mg (4.84 mmol) BPC a little bit at a time. Gas was evolved upon addition of the BPC and the flask became slightly warm. After addition was completed, the mixture was allowed to stir for 20 minutes, then it was filtered and the insoluble solids were washed with 1 mL $CHCl_3$. The combined filtrates were concentrated to give a yellow solid which was dissolved in a minimum of ethyl acetate and purified by flash chromatography using 10% ethyl acetate/90% hexane. A total of 755 mg (86%) white solid oxaziridine (24) (R_f=0.53) were obtained: mp 63.8-64.8° (lit.[6] mp 64-65°); IR (KBr) 3120w, 2970m, 2870w,

2490w, 1940w, 1805w, 1610m, 1520s, 1470m, 1350s, 1315m, 1290m, 1255m, 1245m, 1210m, 1185m, 1105m, 1010w, 915w, 865w, 835s, 820m, 750m, 720m, 690m, cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 8.3 (2H, d, J=8.5 Hz), 7.7 (2H, d, J=8.5 Hz)), 4.7 (1H, s), 1.2 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.9 (quat), 142.8 (quat), 128.6 (CH), 123.6 (CH), 72.3 (CH), 58.9 (quat), 25.2 (CH_3).

Methoxybenzaldehyde-t-butyl imine (**21**) reaction with BPC. Into a 25-mL, round-bottom flask equipped with magnetic stirrer were added 805 mg (4.21 mmol) of **21** and 10 mL $CHCl_3$. To the stirred solution were carefully added 1.008 g (5.56 mmol) BPC a little bit at a time. Evolution of CO_2 was immediate and the flask became warm. After addition of the BPC was completed, the mixture was allowed to stir for 20 minutes, then filtered and the white solids washed with 2 mL $CHCl_3$. The combined filtrates were concentrated to give a pale yellow semi-solid which was dissolved in a minimum of ethyl acetate and purified by flash chromatography on silica gel, eluting with 5% ethyl acetate/95% hexane. A total of 699 mg (80%) clear, pale amber liquid was obtained (R_f=0.54) which was the oxaziridine (25): IR 2980m, 1615m, 1515m, 1390w, 1360w, 1250s, 1170m, 1035m, 830m cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.4 (2H, d, J=9 Hz), 6.9 (2H, d, J=9 Hz, 4.65 (1H, s), 3.75 (3H, s), 1.15 (9H, s).

Acetone methylphenylhydrazone reaction with BPC. A 50-mL, round-bottom flask was equipped with magnetic stirrer. To the flask were added 811.2 mg (5.00 mmol) acetone methylphenylhydrazone[40] and 10.0 mL $CHCl_3$. To the clear, colorless solution were slowly added 996.3 mg (5.50 mmol) BPC, a little bit at a time, over a

period of seven minutes. The reaction was immediate and exothermic with the vigorous evolution of gas. After 30 minutes at ambient temperature, concentration by rotary evaporation at reduced pressure gave an amber solid which was purified by flash chromatography using silica gel and eluting with 10% ethyl acetate/90% hexane. There were obtained 224.5 mg (37%) pale amber solid (R_f=0.62) which was 1,4-dimethyl-1,4-diphenyl-2-tetrazine mp 138.3-140.0° (lit.[41] mp 141-142°): IR (KBr) 3050w, 2930w, 1590s, 1490s, 1450m, 1430m, 1195m, 1175m, 1150w, 1090s, 1020m, 995m, 880m, 750m, 740s, 685s, 615m, 605w, 520w cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33-7.21 (m, 4H), 6.92 (t of t, 1H, J=7.0 and 1.4 Hz), 3.45 (s, 3H, NCH_3); MS (m/e) 240 (M^+, 36), 212(1), 197(3), 120(6), 106(100), 77(65), 51(12).

There were also obtained 107.9 mg (16%) amber liquid (R_f=0.39) which was N-methyl-N-nitrosoaniline[42] and 159.8 mg (20%) amber liquid (R_f=0.2) which was recovered acetone methylphenylhydrazone.

Benzaldehyde methylphenylhydrazone reaction with excess BPC. Into a 100-mL, three-necked, round-bottom flask equipped with magnetic stirrer, reflux condenser and nitrogen inlet stopcock, were added 25 mL $CHCl_3$ and 2.10 g (0.0100 mmol) benzaldehyde methylphenylhydrazone. To the chloroformic solution, at room temperature while stirring, were added in small portions an excess of BPC amounting to 4.75 g (0.0288 mol). Upon addition of BPC, reaction was immediate with the liberation of gases and heat. When addition of BPC was completed, the reaction mixture was allowed to stir overnight. The insoluble white solid (benzamide) produced in the reaction was filtered off. The solvent was then taken off in vacuo and

the residue was dissolved in CH_2Cl_2. The solution was subjected to column chromatography using neutral alumina and eluting with CH_2Cl_2. The solvent was taken off in the first fraction leaving 1.12 g of a residue. 100 mg of this residue was subjected to flash chromatography using silica gel and eluting with hexane. In the first fraction appeared a yellow oil (75.3 mg) which on the basis of TLC seemed to be a pure compound. The second fraction (11.0 mg) contained some of this compound in addition to other materials. Some of the compound of the first fraction was further purified by preparative TLC using silica gel and eluting with hexane. The pure compound obtained was identified as azoxybenzene: IR (melt) 3067w, 1482s, 1438s, 1329w, 1300m, 1275w, 1163w, 1070m, 1024m, 763s, 684s cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.33(2H, m), 8.16(2H, m), 7.50 (6H,m), M δ (m/e), 198(M^+, 15), 169(10), 141(8), 115(5), 105(11), 91(20), 77(100), 65(30), 51(55), 39(21).

N-4-Nitrobenzyliden-N'-4-methoxybenzylidenazine reaction with BPC in the presence of excess p-toluic acid. Into a 10-mL, round-bottom flask equipped with magnetic stirring, were added 849 mg (3.00 mmol) of the mixed azine, 2040 mg (15 mmol) p-toluic acid and 5 mL $CDCl_3$. To this mixture was added 840 mg (4.50 mmol) BPC. The mixture was warmed to 40 °C in order to accelerate the reaction. Gases were given off. The mixture was kept at 40 °C with stirring for two hours and then at room temperture overnight. Then the insoluble solids were separated by filtration. The chloroformic solution was extracted with aqueous $NaHCO_3$ until all the unreacted p-toluic acid was removed and then the solution was dried with anhydrous $MgSO_4$. The solvent was taken off in vacuo and the residue was taken up in hexane

filtering off a small amount of an insoluble orange solid. Evaporation of the hexane left 765 mg of a residue. To this residue was added 389 mg (2.70 mmol) dimethyl maleate as an internal standard; the mixture was dissolved in some $CDCl_3$ and a 300 MHz ^1H NMR spectrum was taken. Table 4-1 shows the calculated yields of the products.

N-Cyclohexyliden-N'-4-nitrobenzylidenazine reaction with BPC in the presence of excess p-toluic acid. Into a 10-mL, round-bottom flask equipped with magnetic stirring, were added 100 mg (0.408 mmol) of the mixed azine, 278 mg (2.04 mmol) p-toluic acid and 2 mL $CDCl_3$. To this solution was added 114 mg (0.612 mmol) BPC in two portions. Gases were given off. The mixture was then allowed to stir at room temperature overnight. The insoluble solids were filtered off and 50 mg (0.266 mmol) 1,2-dibromoethane were added to the chloroformic solution as an internal standard. A 300 MHz ^1H NMR spectrum was taken of this solution. Table 5-1 shows the calculated yields of the products.

Symmetrical azines reaction with BPC in the presence of excess of a carboxylic acid. The open-chain azines were prepared by the methods of Pross and Sternhell[43] or Barton et al.[44] The cyclic azines were prepared by the method of Williams and Dolbier[1a] for the syntheses of **5**.

0.0100 mol of the azine and 0.0200 mol of the carboxylic acid were dissolved in 50 mL $CHCl_3$. To this solution, at room temperature, while stirring magnetically, was added 3.39 g BPC in portions. The $CHCl_3$ reaction mixture was then extracted with a saturated aqueous $NaHCO_3$ solution until all the unreacted carboxylic was

taken out. The chloroformic solution was dried with anhydrous $MgSO_4$ and then the solvent was taken off in vacuo. The residue was taken up in hexane and the solid benzamide was filtered out. The hexane was then evaporated in vacuo. Column chromatography of the residue on silica gel allowed the separation of the ester usually as the first fraction.

The various esters were identified, on the basis of their IR and ^1H NMR spectra.[11,18] For p-methoxybenzyl p-toluate the ^1H NMR spectrum was: (300 MHz, $CDCl_3$) δ 7.96 (2H, m), 7.37 (2H, m), 7.21 (2H, m), 6.89 (2H, m), 5.27 (2H, s), 3.77 (3H, s), 2.38 (3H, s).

Benzaldehyde azine (**1b**) reaction with MCPBA. A 10-mL, round-bottom flask was equipped with magnetic stirrer and pressure-equalizing addition funnel. To the flask were added 59.5 mg (0.286 mmol) **1b**, 7.1 mg (0.031 mmol) benzyltriethylammonium chloride, 0.50 mL $CDCl_3$ and 2.00 mL saturated aqueous sodium bicarbonate. A solution of 148 mg (0.686 mmol) 80-85% m-chloroperoxybenzoic acid (MCPBA) in 2.0 mL $CDCl_3$ was added over a period of four minutes. After stirring for two hours at ambient temperature, the organic layer was separated and dried over anhydrous sodium sulfate. To the solution were added 43.6 mg (0.3025 mmol) dimethylmaleate as internal standard and the ^1H NMR (300 MHz) was taken. The absolute yields were determined by integration of the benzaldehyde resonance at 10.01 ppm, the benzaldehyde azine oxide resonance at 9.41 ppm and the benzaldehyde azine resonance at 8.66 ppm relative to the dimethylmaleate resonance at 6.22 ppm. There were obtained 0.9755 mmol (17.1%) benzaldehyde, 0.02465 mmol

(8.6%) benzaldehyde azine oxide, and 0.09577 mmol (33.5%) benzaldehyde azine remained unreacted.

Benzaldehyde azine (**1b**) reaction with dimethyldioxirane. Into a small vial were weighed 5.0 mg (0.0240 mmol) 1b. To the vial were added 1.00 mL (0.055 mmol) of a 0.055 M acetone-d_6 solution of dimethyldioxirane-d_6 prepared according to the literature.[45] The clear, colorless solution was added to a small vial containing 6.2 mg (0.0430 mmol) dimethylmaleate as internal standard and the ^{1}H NMR (300 MHz) was taken. Integration of the benzaldehyde resonance at 10.06 ppm, the benzaldehyde azine oxide resonance at 9.41 ppm and the benzaldehyde azine resonance at 8.70 ppm relative to the dimethylmaleate internal standard at 6.41 ppm gave the abolute yields. There were obtained 0.0161 mmol (33%) benzaldehyde, 0.00243 mmol (10%) benzaldehyde azine oxide, and there remained 0.0113 mmol (47%) benzaldehyde azine.

Benzaldehyde azine (**1b**) reaction with 2-tolylsulphonyl-3-phenyloxaziridine. Into a 25-mL, three-necked, round-bottom flask equipped with magnetic stirrer, reflux condenser and nitrogen inlet stopcock, were added 124.8 mg (0.600 mmol) benzaldazine, 2.0 mL $CDCl_3$ and 165 mg (0.600 mol) 2-tolylsulphonyl-3-phenyloxaziridine.[46] The stirred solution was warmed to 40-45 °C and kept for 20 hours. After this time, all the oxaziridine had reacted as checked by ^{1}H NMR by the disappearance of the C-H oxaziridine proton at δ 5.4. However, the ^{1}H NMR spectrum showed that there was some unreacted azine present. Another equivalent of the oxaziridine (0.600 mmol) was added to the reaction mixture and it was warmed to

50 °C. The reaction mixture was kept at this temperature with stirring overnight. Then 60.0 mg (0.416 mmol) dimethyl maleate was added to the reaction mixture as an internal standard. Integration of the 300 MHz NMR spectrum gave 9.4 for the two vinylic protons of dimethyl maleate and 12.4 for the benzaldehyde proton. This translates to an NMR yield of 91.5% for benzaldehyde.

Since there was the possibility that some benzaldehyde might have derived from the 2-tolylsulphonyl-3-phenyloxaziridine, the above reaction was repeated but using anisaldehyde azine instead of benzaldehyde azine. The ^{1}H NMR spectrum of the final reaction mixture showed that both anisaldehyde and benzaldehyde formed in the reaction. 0.300 mmol of p-nitrobenzaldehyde was added in this case to the final reaction mixture as an internal standard. Integration of the 200 MHz NMR spectrum gave 10.7 for the p-nitrobenzaldehyde proton and 23.9 for the anisaldehyde proton. This translates to an NMR yield of 67.0% for anisaldehyde.

In the 2-tolylsulphonyl-3-phenyloxaziridine oxidation of benzaldazine, no azine monoxide product formed as seen from the ^{1}H NMR spectrum.

APPENDIX
ACRONYMS USED IN THIS DISSERTATION

BPC	N-Benzoylperoxycarbamic Acid
DMF	N,N-Dimethylformamide
IR	Infrared
MCPBA	Meta-chloroperbenzoic Acid
NMR	Nuclear Magnetic Resonance
MS	Mass Spectrometry
THF	Tetrahydrofuran
TLC	Thin-Layer Chromatography
TMS	Tetramethylsilane

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BIOGRAPHICAL SKETCH

Rodrigo Paredes (Rod) was born on May 25, 1934, in Popayan, Colombia, where he attended primary and secondary school. Upon graduation from high school in 1953, Rod attended the University of Florida where he obtained a BSChem in 1958 and later on began graduate studies toward a PhD. In 1962, while visiting Colombia, Rod was offered a teaching position at the Universidad del Valle in Cali, then the fastest growing and most promising university in Colombia largely through the aid received from U.S. foundations such as the Rockefeller and Ford Foundations. Since Rod did not want to miss the opportunity of joining the Universidad del Valle, he chose to obtain a MS and return to Colombia. In June 1963, Rod joined the faculty of the Chemistry Department in the Chemical Engineering School of the Universidad del Valle. Rod was the first chemist on the Chemistry Department staff since all the other members were then chemical engineers. The rapid growth of the Universidad del Valle at that time required the establishment of a Science School. In 1966, the Science School was created at the Universidad del Valle incorporating the Biology, Chemisry, Mathematics and Physics Departments. In 1966, Rod became Chairman of the Chemistry Department, a position he held for five years. During this time, Rod strove to pursue the development of the Chemistry Department mainly by improving its infrastructure and by forming native teaching and research faculty by sending the most promising chemistry graduates to U.S. universities to pursue graduate studies

with Rockefeller and Ford Foundations' scholarships. Unfortunately, the political turmoil in the Universidad del Valle and other factors restrained the development during the 1970s. In spite of many vicissitudes and problems during the 1970s and 1980s, the Chemistry Department developed into one of the best in Colombia. In 1974, a MS program in chemistry was started. Rod has directed the research work of nine MS graduates at the Universidad del Valle. In 1971, Rod did his sabbatical with Dr. William R. Dolbier, Jr. at the University of Florida. Ever since then, Rod has continued to work with Dr. Dolbier in collaborative research projects. This dissertation is based on the main results obtained in the azine collaborative research project.

Rod is a candidate for the PhD degree in December, 1991, at the ripe age of 57. Upon graduation, Rod plans to continue his research efforts in collaboration with Dr. Dolbier. In the near future, they hope to be able to direct the research of doctoral candidates in the Universidad del Valle.

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

William R. Dolbier, Jr., Chairman
Professor of Chemistry

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Alan R. Katritzky
Kenan Professor of Organic Chemistry

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Eric Enholm
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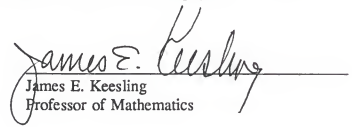

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This dissertation was submitted to the Graduate Faculty of the Department of Chemistry in the College of Liberal Arts and Sciences and to the Graduate School and was accepted as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

December, 1991

Dean, Graduate School